REMARKS

IDS

The Examiner indicates that no 1449 form is found to acknowledge consideration of the prior art. Attached is a copy of the 1449 sent with the IDS filed on July 25, 2002.

Also attached is a new Information Disclosure Statement directed to US 6,495,557, which is an equivalent to DE 198 19 023 cited in the earlier Information Disclosure Statement dated July 25, 2002.

Amendments

The claims are amended. The rejections to the form of the claims under 35 USC § 112, second paragraph, and under § 101 are moot.

The Office Action alleges that the term "potency disorders" is too vague. Applicants respectfully disagree. One of ordinary skill in the art readily understands the scope and meaning of the term. Thus, it is not indefinite. Furthermore, the specification further provides as examples, erectile dysfunction, and also impotence. See page 2, lines 30-37.

The 37 CFR 1.475 Issue

The Examiner alleges that rule 475 "makes clear" that once a compound claim is determined to have allowable subject matter, applicants are "entitled to have, at most, one use of those compounds and one method of making those compounds."

Applicants respectfully disagree. Rule 475 relates to the unity of invention requirement. No allegation has been made that the claims relate to inventions that do not satisfy the requirements of the unity of invention requirement.

Additionally, nowhere does the rule state that applicants are "entitled to have, at most, one use of those compounds and one method of making those compounds." Section (d) of the rule appears to have the closest language to the language of the allegation and said section states that:

> If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each of the other categories related thereto will be considered as the main invention in the claims, see PCT Article 17(3)(a) and § 1.476(c).

This language directs the International Search Authority to search the "main invention" only after lack of unity of invention is determined and no additional searching fees are paid. If

additional searching fees are paid, more than one invention is searched. This language does not state or mean that at most one use and one method of making claims will be searched.

Reconsideration is requested.

The Utility Rejection under 35 USC § 101

The Office action alleges that claim 7 does not satisfy the specific utility requirements. Claim 7, now rewritten as claims 10, 11, 16 and 17 is directed to inhibiting phosphodiesterase V.

Applicants respectfully disagree. The specification teaches that inhibition of phosphodiesterase V is related to the treatment of cardiovascular diseases, such as cardiac insufficiency, and for the treatment and/or therapy of potency disorders, such as erectile dysfunction. See specification, for example, on page 2, lines 11-37, and page 11, lines 18-26. Thus, the inhibition of phosphodiesterase V is a specific utility that provides a benefit to the public.

Courts have repeatedly found that even the mere identification of a pharmacological activity of a compound provides an "immediate benefit to the public" and thus satisfies the utility requirement. See *Nelson v. Bowler*, 626 F.2d 853, 206 USPQ 881 (CCPA 1980), where the invention related to compounds having an in vitro activity, which had a recognized value in pharmacology at the time the application was filed. Applicants also bring the attention of the Examiner to *Cross v. Iizuka*, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), where the invention was a chemical compound having a disclosed in vitro activity held to sufficiently disclose a pharmacological utility for the compounds. Likewise here, applicants sufficiently disclose a utility, which provides an "immediate benefit to the public" and thus the invention satisfies the utility requirement.

Reconsideration is respectfully requested.

The Rejection Under 35 USC § 103

The Office Action alleges that forming a composition is obvious "since the time of Alchemists working in caves." That may be so, but forming a pharmaceutical composition containing a compound of claim 1 is not obvious. Claim 4 is dependent on claim 1, against which no prior art rejection is made. Claims dependent from an otherwise allowable claim should also be found allowable.

The Rejection Under 35 USC § 112, first paragraph

The Office Action rejects claim 6 and states that it should be limited to one use since it is not believable, on its face, that any one compound could have all of those uses.

Applicants respectfully disagree. The claim was, directed to potency disorders and diseases of the cardiovascular system. The subject matter of claim 6 now appears in several new claims. The specification on page 11, lines 18-26 teaches that

> The compounds of the formula I and their physiologically acceptable salts can be employed in the control of diseases in which an increase in the cGMP (cyclic guanosin monophosphate) level leads to inhibition or prevention of inflammation and muscle relaxation. The compounds according to the invention can particularly be used in the treatment of diseases of the cardiovascular system and for the treatment and/or therapy of potency disorders.

One of ordinary skill in the art therefore would understand that both of the claimed groups of diseases are related to cGMP, and thus, a compound which would have an effect on cGMP would affect both group of diseases. There is nothing unbelievable, on its face, here.

Additionally, the relationship of cardiovascular diseases and potency disorders to cGMP have been known in the prior art. See, for example, US 5,981,527, titled "Cyclic GMP-specific phosphodiesterase inhibitors" assigned to ICOS Corporation, and also US 6,087,368, titled "Quinazolinone inhibitors of *cGMP* phosphodiesterase" assigned to Bristol-Myers Squibb Company, both predating the earliest priority date of the present application.

Applicants additionally teach on page 2, line 37 to page 3, line 7 that:

> The compounds are effective as inhibitors of the phenylephrine-induced contractions in corpus cavernosum preparations of hares. This biological action can be demonstrated, for example, according to the method which is described by F. Holmquist et al. in J. Urol., 150, 1310-1315 (1993).
> The inhibition of the contraction shows the efficacy of the compounds according to the invention for the therapy and/or treatment of potency disorders.

Thus, there cannot be doubt that the compounds are useful as stated.

Nevertheless, applicants point out that the courts have placed the burden upon the PTO to provide **evidence** that sheds doubt on the disclosure that the invention can be made and used as stated. The disclosure "*must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statement contained therein, which must be relied on for enabling support." See *In re Marzocchi*, 439 F.2d 220, 169 USPQ 367 (CCPA 1971). No such evidence or reason for doubting Applicants' disclosure is provided.

Doubt has been held reasonable where, for example, the invention has been characterized as "highly unusual," *In re Houghton*, 433 F.2d 820 (CCPA 1970), as "incredible," *In re Citron*, 325 F.2d 248, (CCPA 1963), or as "too speculative," *In re Eltgroth*, 419 F.2d 918 (CCPA 1970). The treatment by the same compound of two groups of diseases/disorders that are related by cGMP as discussed above is not "highly unusual," "incredible," and/or "too speculative." Thus, the rejection should be withdrawn for this reason alone.

With respect to the array of diseases, the Patent Office has not provided any reason why one of ordinary skill in the art would not be able, through routine screening and testing, to determine which of the synthesized compounds according to the claims possesses beneficial properties to any of the specific diseases encompasses by the claims. Screening and testing of thousands of compounds in a variety of assays in the field of pharmaceutical art is routine, and thus, does not constitute undue experimentation, especially in view of the guidance provided by the specification on page 2, line 16 to page 3, line 4, wherein applicants cite to several references that teach how to test the activity levels of the claimed compounds.

Any one of the claimed compounds can be tested by routine protocol known to those of ordinary skill in the art and has a reasonable expectation of success. It would require only routine effort to take any one of the compounds and test its activity on any disease falling into the group of diseases claimed or on a specifically named disease. As stated by the court in *In re Wands*, 858 F.24 731, 8 USPQ2d 1400 (Fed. Cir. 1988), "a considerable amount of experimentation is permissible, if it is merely routine or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed," which is the case here.

The Office Action alleges that even if the uses were believable, it would require undue experimentation to determine what host - dosage relationship would produce what results.

The Federal Circuit in *Cross,* supra, affirmed a USPTO Board of Patent Interferences decision on whether dosage levels need to be disclosed for a pharmaceutical in order to enable it. The Federal Circuit held that where sufficient credible evidence that one skilled in the art, without the exercise of inventive skill or undue experimentation, could determine dosage levels, disclosure of dosage levels is not necessary for enablement.

The Manual of Patent Examination and Procedure, is in accord with the *Cross* decision. The MPEP states that it is unnecessary to disclose dosages to satisfy the enablement requirement.

See, *e.g.*, MPEP 2164.01(c): "it is not necessary to specify the dosage ... if it is known in the art that such information could be obtained without undue experimentation. If one skilled in the art, based on knowledge of compounds having similar physical or biological activity would be able to discern an appropriate dosage ... without undue experimentation, this would be sufficient to satisfy 35 U.S.C. §112, first paragraph."

Nevertheless, applicants did provide doses generically on page 11, lines 27 to 39, and indicated preferences, and factors to consider when determining individual doses. This is more than what is necessary to satisfy the enablement requirement.

Applicants provide ample evidence to the claimed activities and ample guidance to test the activity of specific compounds according to the invention. Any one of the claimed compounds can be tested by routine protocol known to those of ordinary skill in the art, i.e., their testing is does not constitute undue experimentation. Thus, the claims are enabled

Reconsideration is respectfully requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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